REMARKS

Applicant respectfully requests reconsideration.

Claims 87-119 were previously pending in this application.

Claim 117 is cancelled without prejudice or disclaimer. Claims 87 and 118 are amended. Support for these amendments can be found in the specification at least in previously pending claims 117 and 118, the Abstract, Table 2, page 19 lines 19-20, and page 24 lines 19-24.

As a result, claims 87-116, 118 and 119 are pending for examination with claim 87 being the independent claim.

No new matter has been added.

Rejections under 35 U.S.C. §103

Claims 87-111 and 117-119 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nyberg (5,677,472) in view of Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination. Applicant respectfully traverses the rejection in part.

The rejection in view of the primary reference Nyberg and the secondary references Kissel, Papahadjopoulos, Lenk and Kikuchi has been addressed by Applicant in at least the response filed on October 18, 2010. Applicant requests that the Examiner take those arguments into consideration together with the arguments provided herein, as these previous arguments will be only briefly summarized herein.

At the outset, Applicant again notes that the rejection is premised on a primary reference (Nyberg) that teaches separation and isolation of a phospholipid from a naturally occurring material that comprises a number of phospholipids and other components. Nyberg stresses the importance of isolating sphingomyelin throughout the patent. For example, Nyberg states that "For the possible applications of sphingomyelin it is most important that sphingomyelin can be extracted in a form which is as pure as possible, and essentially free from other phospholipids." (col 1 lines 64-67, emphasis added). Nyberg also clearly states that its method is intended to separate sphingomyelin from other phospholipids. For example, Nyberg states that "The inventive method for extracting sphingomyelin is based on the fact that the solubility of sphingomyelins in a mixture of an organic solvent of intermediate polarity and an essentially

non-polar organic solvent is lower than for the other phospholipids in the mixture." (col 5 lines 19-23, emphasis added.) Nyberg further states that "The principle for isolating sphingomyelin thus is to add to a mixture of neutral fat and phospholipids dissolved in an essentially non-polar organic solvent, an organic solvent of intermediate polarity in a suitable amount, whereby sphingomyelins precipitate, while the other phospholipids and neutral fat remain dissolved." (col 5 lines 24-29, emphasis added.)

The desired result of the Nyberg method therefore is opposite to the desired result of the instant claims (i.e., Nyberg's method selectively removes and harvests a phospholipid from a mixture while the method of the instant claims combines phospholipids to form a lipid blend and a lipid suspension). In view of Nyberg's stated purpose of deliberately extracting a phospholipid, sphingomyelin, from a mixture, one of ordinary skill in the art looking to combine phospholipids into a lipid blend would not look to such a reference. More importantly, one of ordinary skill in the art would not have a reasonable expectation of success for making a lipid blend based on Nyberg's expressly stated purpose of selectively separating and isolating the phospholipid sphingomyelin from a lipid mixture.

With respect to the specific limitations of the rejected claims, the Examiner maintains that Nyberg discloses steps (a) to (c) of claim 87. Applicant disagrees. Steps (a) to (c) of claim 87 require (a) dissolving phospholipids in a first non-aqueous solvent to form a lipid solution, (b) then precipitating a lipid blend comprising the phospholipids out of the lipid solution using a second non-aqueous solvent, and (c) then collecting the lipid blend. Claim 87 is now amended to recite that the starting phospholipids are DPPA, DPPC and MPEG5000-DPPE. The steps yield, as an intermediate, a lipid blend that comprises all three starting phospholipids.

The method of Nyberg differs from these recited steps in a number of ways. First, Nyberg's starting material is different from the starting material of claim 87. Specifically, Nyberg's starting material is a naturally occurring composition that necessarily comprises sphingomyelin and that may (but need not) comprise phosphatidylcholine and phosphatidylethanolamine. The starting material of claim 87 necessarily comprises DPPA, DPPC, and non-naturally occurring MPEG5000-DPPE, and it lacks sphingomyelin. This latter distinction alone calls into question the relevance of the Nyberg method to the claimed invention.

Second, since Nyberg's method intends to extract and enrich a single select phospholipid (i.e., sphingomyelin), its solvents and conditions are particularly chosen based on their ability to maximize sphingomyelin extraction from the starting material. Nyberg dissolves its starting material in a mixture of an essentially non-polar organic solvent (e.g., heptane) and an essentially polar organic solvent (e.g., ethanol), then performs a phase separation to selectively remove the polar organic solvent phase, and then adds, to the remaining non-polar organic solvent phase, an organic solvent of intermediate polarity (e.g., acetone) to precipitate out primarily sphingomyelin. In contrast, step (b) of claim 87 precipitates out the intermediate lipid blend comprising all three starting phospholipids. More specifically, the second non-aqueous solvent of claim 87 is a solvent that indiscriminately precipitates out all three starting phospholipids.

Third, the desired product from Nyberg's method is a precipitate that is significantly enriched for sphingomyelin and is depleted for phosphatidylcholine or phosphatidylethanolamine. In contrast, the lipid blend solid collected at step (c) of claim 87 is neither significantly enriched nor significantly depleted of any of the starting phospholipids. Notably, in Nyberg's method, phosphatidylcholine and phosphatidylethanolamine (if present in the starting material) is found primarily in the "brown phase" and the supernatant. However, Nyberg provides no guidance as to how to further process the "brown phase," nor does it provide any motivation to do so.

Nyberg therefore does not, and could not, meet the limitations of steps (a) to (c) of claim 87, namely precipitating out and collecting a solid lipid blend comprising DPPA, DPPC and MPEG5000-DPPE. For this reason, a prima facie case of obviousness has not been made. Nevertheless, for the sake of completeness, Applicant also addresses the Examiner's position regarding the secondary references.

The Examiner relies on the secondary references Kissel, Papahadjopoulos, Lenk and Kikuchi as teaching steps (d) and (e) of claim 87. The Examiner states that it would have been obvious to combine the teachings of Nyberg with those of the secondary references Kissel, Papahadjopoulos and Lenk "if lipid encapsulation of an active agent is desired." The Examiner's rationale is insufficient as a basis to combine Nyberg with the secondary references because the claimed invention does not relate to encapsulation of an active agent as provided by the secondary references. The instant application instead teaches that the lipid suspension is

useful as an ultrasound contrast agent particularly when combined with a perfluorocarbon gas. Accordingly, the Examiner's proffered rationale for combining the Nyberg reference with the Kissel, Papahadjopoulos and Lenk references (and presumably also the Kikuchi reference) fails because the motivation to lipid encapsulate active agents is not relevant to the claimed invention.

One of ordinary skill in the art would not look to these references if the intent was to prepare an ultrasound contrast agent. The Examiner acknowledges as much when he states that Nyberg, Kissel, Papahadjopoulos, Lenk and Kikuchi "do not teach how to prepare liposomes containing ultrasound contrast agents containing perfluoropropane." (See instant office action, page 8, first full paragraph.) Applicant agrees and, in an earnest effort to expedite prosecution, has amended claim 87 to recite that the lipid suspension with a perfluorocarbon gas is an ultrasound contrast agent. For these reasons also, the prima facie burden has not been met.

The Examiner further states that "the secondary references clearly show that the liposomes are formed by dissolving the phospholipids in an organic solvent and mixing with an aqueous medium." However, the Examiner fails to discuss with any specificity how one of ordinary skill in the art would combine the Nyberg teachings with those of the secondary references, including in particular how the final products from Nyberg's methods are to be used in the methods of the secondary references. For example, if the sphingomyelin-enriched precipitate is used as a starting material in the methods of the secondary references, then this would not yield the lipid suspension of DPPA, DPPC and DPPE-MPEG5000 of claim 87. It is also clear that Nyberg's "brown phase" cannot be used as the starting material in the methods of the secondary references particularly since the Examiner acknowledges that those references teach "the use of pure phospholipids" for the preparation of liposomes. (Instant office action, page 12, first full paragraph, emphasis added.) The use of the "brown phase" is not use of "pure phospholipids." Accordingly, Nyberg's final products are either unsuitable as starting materials in the methods of the secondary references, or their use in those methods does not yield the lipid blend of claim 87.

The Examiner's failure to explain with any particularity how the primary reference and secondary references are to be combined prevents Applicant from providing a complete rebuttal to the rejection. Nevertheless, Applicant in good faith attempts to address the deficiencies in the secondary references. Kissel, Papahadjopoulos and Lenk all teach the need to remove the final

organic solvent prior to addition of the final aqueous solution. Steps (d) and (e) of claim 87, as now amended, however recite that the lipid suspension retains the third non-aqueous solvent. In addition, Lenk also teaches that "the amount of lipid must be sufficient so as to exceed that amount needed to coat the emulsion droplets (about 40 mg of lipid per ml of aqueous phase)." (Col 6, lines 40-43, emphasis added.) Claims 99 and 119 recite a lipid suspension having about 0.75 to 1.0 mg/ml of lipid blend in the lipid suspension, a concentration that is far below that required by Lenk. Lenk teaches away from such low concentrations of lipids, and therefore one of ordinary skill in the art would not have a reasonable expectation of success regarding the use of lower lipid concentrations such as those recited in claims 99 and 119.

The Examiner has further maintained that there is no experimental data to evidence the improved products obtained using the claimed method. Applicant notes that the instant specification describes the advantages of the claimed method as compared to prior art methods. (Page 12 lines 1-21.) In addition, the specification teaches that when compared to prior art methods, the claimed method results in increased yield and more uniform lipid blend. Specifically, the prior art methods resulted in a loss of lipids ranging from 12 to 48%. (Page 23 line 20 through to page 24 line 6.) This loss was attributed in part to the wide range of particle sizes that are obtained using the prior art methods (i.e., 0.6 to 100 microns). (Page 2 lines 9-19.) In contrast, the claimed methods result in full recovery of lipids and a smaller and more uniform particle size (i.e., less than 50 nm). (Page 24 lines 7-17.)

A prima facie case of obviousness has not been made based on the combination of Nyberg in view of Kissel, Papahadjopoulos, Lenk or Kikuchi. One of ordinary skill in the art would have had no reason to refer to and/or to combine the primary and secondary references, for the reasons listed above. For those same reasons, one of ordinary skill in the art would not have had a reasonable expectation of success regarding such combination and/or modification of the reference teachings. Even if made, the combination does not yield all the limitations of the rejected claims. And finally, the instant specification provides experimental data to show the benefits of the claimed method.

For all of the foregoing reasons, the rejected claims are not rendered obvious by the combination of Nyberg in view of Kissel, Papahadjopoulos, Lenk or Kikuchi. Reconsideration and withdrawal of the rejection is requested.

Claims 111-114 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nyberg (5,677,472) in view of Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination, further in view of Swaerd-Nordmo (6,165,442). Applicant respectfully traverses the rejection.

Swaerd-Nordmo is not prior art to the instant application because its effective filing date for prior art purposes (i.e., its 35 U.S.C. 102(e) date) is May 14, 1998 which is after the filing date of the priority application of the instant application (i.e., January 14, 1998). (MPEP 706.02(f)(1), particularly Example 9.)

The rejection therefore is reduced to the teachings of Nyberg in combination with Kissel, Papahadjopoulos, Lenk or Kikuchi. The Examiner acknowledges however that claims 111-114 are not rendered obvious by the combination of Nyberg with Kissel, Papahadjopoulos, Lenk or Kikuchi by his reliance on Swaerd-Nordmo for this teaching and by his explicit statement that the Nyberg, Kissel, Papahadjopoulos, Lenk and Kikuchi references "do not teach how to prepare liposomes containing ultrasound contrast agents containing perfluoropropane." (Instant office action, page 8, first full paragraph.)

Accordingly, the rejected claims are not rendered obvious by these references. Reconsideration and withdrawal of the rejection is requested.

Claims 115 and116 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nyberg (5,677,472) in view of Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination, in view of Swaerd-Nordmo (6,165,442), further in view of Unger (6,071,495). Applicant respectfully traverses the rejection in part.

The rejected claims 115-116 depend from claim 112, which depends from claim 87. As discussed above, a prima facie case of obviousness of claim 87 has not been made, at least because there is no rationale for combining Nyberg with Kissel, Papahadjopoulos, Lenk or Kikuchi and, even if made, the combination does not provide all the limitations of claim 87. Also as discussed above, Swaerd-Nordmo is not prior art against the instant application as its 35 U.S.C. 102(e) date is after the priority date of the instant application. Unger does not cure the

deficiencies in the combination of Nyberg with Kissel, Papahadjopoulos, Lenk or Kikuchi, including the missing rationale for combining Nyberg with Kissel, Papahadjopoulos, Lenk or Kikuchi.

Accordingly, the combination of Nyberg with Kissel, Papahadjopoulos, Lenk or Kikuchi, in view of Unger '495 does not render obvious the rejected claims. Reconsideration and withdrawal of the rejection is requested.

Claims 117-119 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nyberg (5,677,472) in view of Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination, further in view of Unger (6,416,740). Applicant respectfully traverses the rejection in part.

The rejected claims 117-119 depend from claim 87. As discussed above, a prima facie case of obviousness of claim 87 has not been made, at least because there is no rationale for combining Nyberg with Kissel, Papahadjopoulos, Lenk or Kikuchi and, even if made, the combination does not provide all the limitations of claim 87. Unger '740 does not cure the deficiencies in the combination of Nyberg with Kissel, Papahadjopoulos, Lenk or Kikuchi, including the missing rationale for combining Nyberg with Kissel, Papahadjopoulos, Lenk or Kikuchi. The Examiner relies upon Unger '740 for the teaching of the lipid combination of DPPA, DPPC and DPPE-PEG5000. However, the Examiner does not indicate how this teaching by Unger '740 is to be combined with the method of Nyberg that requires a starting material that minimally must comprise sphingomyelin. One of ordinary skill in the art would have no reason to combine the teachings of Nyberg, which relate to isolation of sphingomyelin, with certain select teachings of Unger '740 relating to the particular lipid combination consisting of DPPA, DPPC and DPPE-PEG5000 and lacking sphingomyelin. Applicant further notes that claim 87 recites MPEG5000-DPPE.

For all of the foregoing reasons, Nyberg in view of Kissel, Papahadjopoulos, Lenk or Kikuchi, and in further view of Unger '740 does not render obvious the rejected claims. Reconsideration and withdrawal of the rejection is requested.

Claims 87-111 are rejected under 35 U.S.C. §103(a) as being unpatentable over Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination. Applicant respectfully traverses the rejection in part.

The Examiner has acknowledged that Kissel, Papahadjopoulos, Lenk and Kikuchi "do not teach how to prepare liposomes containing ultrasound contrast agents containing perfluoropropane." (Instant office action, page 8, first full paragraph.) Claim 87, as now amended, recites that the lipid suspension with a perfluorocarbon gas is an ultrasound contrast agent. This teaching is not found in these references, as acknowledged by the Examiner.

Claim 87, as now amended, also recites that the lipids are DPPA, DPPC and MPEG5000-DPPE. This combination of lipids is also not found in these references. This deficiency is also acknowledged by the Examiner since claim 117 as previously pending, which recited these three phospholipids, was not rejected by these references.

Notwithstanding the foregoing, and rather for the record, Applicant further traverses the rejection because the references, whether taken individually or in combination, do not provide additional limitations of the rejected claims. This is acknowledged by the Examiner. (Instant office action, page 11, fourth full paragraph: "In essence, these references teach steps d and e of claim 87.") The Examiner provides no basis for the teachings of steps (a) to (c) of claim 87, and in so doing the Examiner has failed to meet his burden of a prima facie showing.

With respect to steps (d) and (e) of claim 87, Kissel, Papahadjopoulos and Lenk all teach the need to remove the final organic solvent prior to addition of the final aqueous solution. Steps (d) and (e) of claim 87, as now amended, however recite that the lipid suspension retains the third non-aqueous solvent. In addition, Lenk also teaches that "the amount of lipid must be sufficient so as to exceed that amount needed to coat the emulsion droplets (about 40 mg of lipid per ml of aqueous phase)." (Col 6, lines 40-43, emphasis added.) Claims 99 and 119 recite a lipid suspension having about 0.75 to 1.0 mg/ml of lipid blend in the lipid suspension, a concentration that is far below that required by Lenk. Lenk teaches away from such low concentrations of lipids, and therefore one of ordinary skill in the art would not have a reasonable expectation of success regarding the use of lower lipid concentrations such as those recited in claims 99 and 119.

The Examiner has further maintained that there is no experimental data to evidence the improved products obtained using the claimed method. Applicant notes that the instant specification describes the advantages of the claimed method as compared to prior art methods. (Page 12 lines 1-21.) In addition, the specification teaches that when compared to prior art methods, the claimed method results in increased yield and more uniform lipid blend. Specifically, the prior art methods resulted in a loss of lipids ranging from 12 to 48%. (Page 23 line 20 through to page 24 line 6.) This loss was attributed in part to the wide range of particle sizes that are obtained using the prior art methods (i.e., 0.6 to 100 microns). (Page 2 lines 9-19.) In contrast, the claimed methods result in full recovery of lipids and a smaller and more uniform particle size (i.e., less than 50 nm). (Page 24 lines 7-17.)

A prima facie case of obviousness has not been made based on Kissel, Papahadjopoulos, Lenk or Kikuchi individually or in combination. One of ordinary skill in the art would have had no reason to refer to and/or to combine the references, for the reasons listed above. For those same reasons, one of ordinary skill in the art would not have had a reasonable expectation of success regarding combining or modifying the reference teachings. Even if made, the combination does not yield all the limitations of the rejected claims. And finally, the instant specification provides experimental data to show the benefits of the claimed method.

For all of the foregoing reasons, Kissel, Papahadjopoulos, Lenk and Kikuchi, individually or in combination, do not render obvious the rejected claims. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 117-119 are rejected under 35 U.S.C. §103(a) as being unpatentable over Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination as set forth above, further in view of Unger (WO 96/40285). Applicant respectfully traverses the rejection in part.

The rejected claims 117-119 depend from claim 87. As discussed above, a prima facie case of obviousness of claim 87 has not been made, at least because there is no rationale for combining and/or modifying Kissel, Papahadjopoulos, Lenk or Kikuchi and the references either individually or in combination do not provide all the limitations of claim 87. Unger (WO 96/40285) does not cure these deficiencies. The Examiner relies upon Unger (WO 96/40285) for

the teaching of the lipid combination of DPPA, DPPC and DPPE-PEG5000. However, as now amended, claim 87 recites the lipids DPPA, DPPC and MPEG5000-DPPE. This combination of lipids is not provided Unger (WO 96/40285).

For all of the foregoing reasons, Kissel, Papahadjopoulos, Lenk or Kikuchi, individually or in combination, in further view of Unger (WO 96/40285) do not render obvious the rejected claims. Reconsideration and withdrawal of the rejection is requested.

Claims 87-111 and 117 are rejected under 35 U.S.C. §103(a) as being unpatentable over Munechika (5,662,931) in combination with Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination. Applicant respectfully traverses the rejection in part.

Munechika describes a method for making drug-loaded liposomes. Munechika's method involves dissolving lipids in a first organic solvent (e.g., an ethanol/hexane mixture), removing the first organic solvent to form a residue, dissolving the residue in a second organic solvent (e.g., dichloromethane), and combining that solution with an aqueous solution containing the drug to be encapsulated. This mixture is then emulsified, mixed with another organic solvent (e.g., ethyl acetate), precipitated, and resuspended in another aqueous solution. In contrast, claim 87 recites precipitating its lipid blend in the second non-aqueous solvent, dissolving the precipitate in a third non-aqueous solvent, and then combining it with an aqueous solution to form a final lipid suspension that retains the third non-aqueous solvent. Thus, unlike Munechika which uses an organic solvent to precipitate a lipid-drug complex just prior to the addition of the final aqueous solution, claim 87 precipitates its lipid blend, in the absence of a drug, resuspends that lipid blend in a non-aqueous solvent, and then combines the entire mixture with an aqueous solution.

Munechika does not teach lipid suspensions that can be used as ultrasound contrast agents, and it does not disclose the lipid combination of DPPA, DPPC and MPEG5000-DPPE.

Notably, Munechika teaches that its method "usually" yields liposomes ranging from 10 nm to 50 microns in diameter. That is, Munechika's method prepares liposomes having a broad size range. Applicant has taught that such broad size ranges were observed in the prior art and likely were the cause of decreased lipid yields. The claimed invention overcomes this problem,

as described in the specification, through the preparation of a lipid suspension having more uniform and smaller lipid particle size. One of ordinary skill in the art would not rely on the Munechika reference based on its broad liposome size range and would also not have a reasonable expectation of success.

The teachings of Kissel, Papahadjopoulos, Lenk and Kikuchi are discussed herein. These references do not cure the deficiencies of Munechika.

A prima facie case of obviousness has not been made based on Munechika with Kissel, Papahadjopoulos, Lenk or Kikuchi at least because there is no reasonable expectation of success and not all the limitations of the rejected claims are provided by the combination of references.

For all of the foregoing reasons, the combination of Munechika with Kissel, Papahadjopoulos, Lenk or Kikuchi does not render obvious the rejected claims. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 112-114 are rejected under 35 U.S.C. §103(a) as being unpatentable over Munechika (5,662,931) in combination with Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination, further in view of Swaerd-Nordmo (6,165,442). Applicant respectfully traverses the rejection.

Swaerd-Nordmo is not prior art to the instant application because its effective filing date for prior art purposes (i.e., its 35 U.S.C. 102(e) date) is May 14, 1998 which is after the filing date of the priority application of the instant application (i.e., January 14, 1998). (MPEP 706.02(f)(1), particularly Example 9.)

The rejection therefore is reduced to the teachings of Munechika in combination with Kissel, Papahadjopoulos, Lenk or Kikuchi. The Examiner acknowledges however that claims 112-114 are not rendered obvious by the combination of Munechika with Kissel, Papahadjopoulos, Lenk or Kikuchi by his reliance on Swaerd-Nordmo for this teaching and by his explicit statement that the Munechika, Kissel, Papahadjopoulos, Lenk and Kikuchi references "do not teach how to prepare liposomes containing ultrasound contrast agents containing perfluoropropane." (Instant office action, page 15, second full paragraph.)

Accordingly, the rejected claims are not rendered obvious by these references. Reconsideration and withdrawal of the rejection is requested.

Claims 115-116 are rejected under 35 U.S.C. §103(a) as being unpatentable over Munechika (5,662,931) in combination with Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination in view of Swaerd-Nordmo (6,165,442) as set forth above, further in view of Unger (6,071,495). Applicant respectfully traverses the rejection in part.

The rejected claims 115-116 depend from claim 112, which depends from claim 87. As discussed above, a prima facie case of obviousness has not been made, at least because there is no reasonable expectation of success and the combination of Munechika with Kissel, Papahadjopoulos, Lenk or Kikuchi does not yield all the limitations of claim 87. Swaerd-Nordmo is not prior art against the instant application as its 35 U.S.C. 102(e) date is after the priority date of the instant application. Unger does not cure the deficiencies in the combination of Munechika with Kissel, Papahadjopoulos, Lenk or Kikuchi.

Accordingly, the combination of Munechika with Kissel, Papahadjopoulos, Lenk or Kikuchi, in view of Unger '495 does not render obvious the rejected claims. Reconsideration and withdrawal of the rejection is requested.

Claims 117-119 are rejected under 35 U.S.C. §103(a) as being unpatentable over Munechika (5,662,931) in combination with Kissel (4,863,740) or Papahadjopoulos (4,235,871) or Lenk (4,522,803) or Kikuchi (4,687,661) individually or in combination as set forth above, further in view of Unger (WO 96/40285). Applicant respectfully traverses the rejection in part.

The rejected claims 117-119 depend from claim 87. As discussed above, a prima facie case of obviousness has not been made, at least because there is no reasonable expectation of success and the combination of Munechika with Kissel, Papahadjopoulos, Lenk or Kikuchi does not yield all the limitations of claim 87. Unger (WO 96/40285) does not cure these deficiencies. The Examiner relies upon Unger (WO 96/40285) for the teaching of the lipid combination of DPPA, DPPC and DPPE-PEG5000. Applicant notes that claim 87, as now amended, recites MPEG5000-DPPE.

For all of the foregoing reasons, Munechika in view of Kissel, Papahadjopoulos, Lenk or Kikuchi, individually or in combination, and in further view of Unger (WO 96/40285) do not render obvious the rejected claims. Reconsideration and withdrawal of the rejection is requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. N0469.70022US02.

Respectfully submitted,

/Maria A. Trevisan/_____
Maria A. Trevisan
Registration Number: 48,207
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

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